

U.S. Army Center for Health Promotion and Preventive Medicine

Epidemiologic Consultation No. 29-HE-5711-00 Investigation of an Acute Respiratory Disease Outbreak Due to Adenovirus Type 4 Among Recruits Fort Benning, Georgia April - May 2000

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Readiness Thru Health

U.S. Army Center for Health Promotion and Preventive Medicine

The lineage of the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) can be traced back over 50 years. This organization began as the U.S. Army Industrial Hygiene Laboratory, established during the industrial buildup for World War II, under the direct supervision of the Army Surgeon General. Its original location was at the Johns Hopkins School of Hygiene and Public Health. Its mission was to conduct occupational health surveys and investigations within the Department of Defense's (DOD's) industrial production base. It was staffed with three personnel and had a limited annual operating budget of three thousand dollars.

Most recently, it became internationally known as the U.S. Army Environmental Hygiene Agency (AEHA). Its mission expanded to support worldwide preventive medicine programs of the Army, DOD, and other Federal agencies as directed by the Army Medical Command or the Office of The Surgeon General, through consultations, support services, investigations, on-site visits, and training.

On 1 August 1994, AEHA was redesignated the U.S. Army Center for Health Promotion and Preventive Medicine with a provisional status and a commanding general officer. On 1 October 1995, the nonprovisional status was approved with a mission of providing preventive medicine and health promotion leadership, direction, and services for America's Army.

The organization's quest has always been one of excellence and the provision of quality service. Today, its goal is to be an established world-class center of excellence for achieving and maintaining a fit, healthy, and ready force. To achieve that end, the CHPPM holds firmly to its values which are steeped in rich military heritage:

- ★ *Integrity is the foundation*
 - ★ *Excellence is the standard*
 - ★ *Customer satisfaction is the focus*
 - ★ *Its people are the most valued resource*
 - ★ *Continuous quality improvement is the pathway*

This organization stands on the threshold of even greater challenges and responsibilities. It has been reorganized and reengineered to support the Army of the future. The CHPPM now has three direct support activities located in Fort Meade, Maryland; Fort McPherson, Georgia; and Fitzsimons Army Medical Center, Aurora, Colorado; to provide responsive regional health promotion and preventive medicine support across the U.S. There are also two CHPPM overseas commands in Landstuhl, Germany and Camp Zama, Japan who contribute to the success of CHPPM's increasing global mission. As CHPPM moves into the 21st Century, new programs relating to fitness, health promotion, wellness, and disease surveillance are being added. As always, CHPPM stands firm in its commitment to Army readiness. It is an organization proud of its fine history, yet equally excited about its challenging future.

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<p>13. ABSTRACT (Maximum 200 words)</p> <p>An epidemiological consultation (EPICON) was conducted to investigate an outbreak of acute respiratory disease (ARD) among US Army Infantry trainees at Fort Benning, GA that resulted in the hospitalization of 194 recruits to Martin Army Community Hospital (MACH) between April 23 and May 6, 2000. This outbreak resulted in a ARD admission rate of 2.9% for the week ending April 29, 2000, a six-fold increase over baseline. The average length of stay for all admitted recruits was 2.1 days. All recruits recovered without sequelae; there were no deaths or serious injuries.</p> <p>A case-control study was performed to develop hypotheses regarding the etiology of the outbreak. One unit was chosen for the company. A case was defined as any Infantry trainee who visited a medical facility with a documented fever greater than or equal to 100.4 F (38 C) and at least one ARD symptom. The case-control study group included 288 individuals; all male. 54 trainees met our case definition and 234 individuals were considered controls. Univariate analysis indicated several variables associated with being an ARD case such as assignment to Company D, young age, white race, a history of smoking 6 months prior to training, 5th week of training, recruit crowding in the barracks, higher environmental temperature, and lack of soap in the barracks. Multivariate analysis revealed only sleeping density and white race with becoming an ARD case with a $p < 0.05$. Initially, nasal swab quick tests performed on ill recruits were positive for Influenza A/B but additional laboratory data confirmed that adenovirus (AdV) type 4 was the etiologic agent of the outbreak.</p> <p>Areas for improvement, particularly the ventilation systems, were documented. The most effective intervention for avoiding an AdV outbreak is the oral vaccine; unfortunately, the sole manufacturer ceased production in 1996. Until the vaccine is once again available, outbreaks due to AdV in basic training are inevitable.</p>					
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Executive Summary

Epidemiologic Consultation No. 29-HE-5711-00
Investigation of an Acute Respiratory Disease Outbreak Due to
Adenovirus Type 4 Among Recruits
Fort Benning, Georgia
April – May 2000

An outbreak of acute respiratory disease (ARD) due to adenovirus type 4 resulted in the hospitalization of 194 U.S. Army recruits to Martin Army Community Hospital (MACH) at Fort Benning, GA between 23 April and 6 May 2000. This resulted in an ARD admission rate of 2.9% for the week ending 29 April 2000, a six-fold increase over baseline. The admission of 127 recruits on 26-27 April 2000 overwhelmed MACH and two, 60-man sleeping bays were converted to sick bays in the most heavily affected unit. The average length of stay for all admitted recruits was 2.1 days. All recruits recovered without sequelae; there were no deaths or serious complications.

The Epidemiologic Consultation (EPICON) investigation reviewed administrative, military, environmental, and medical information. No concerns with medical treatment or medical-inprocessing procedures were found. The outbreak was heavily concentrated to one company that had an admission rate of 58.6% for the 2-week period. A case-control study was performed on this company and a different company from the same battalion (and barracks). Young age (≤ 20 years), white race, a history of smoking in the 6 months prior to training, higher environmental temperatures ($> 72^{\circ}\text{F}$), recruit crowding in the barracks (≥ 50 recruits per bay), and lack of soap in the barracks lavatory were found to be associated with ARD on univariate analysis. Of these variables, however, only smoking and recruit crowding were found to be associated with disease on multivariate analysis. Areas for improvement in the environment, particularly the ventilation systems of the 'starship' barracks, to conform to the standards of the American Society of Heating, Refrigerating, and Air-Conditioning Engineers, Inc. (ASHRAE) [1] were documented.

This is the third EPICON in 4 years (1997, 1998, and 2000) describing a significant adenovirus outbreak among U.S. Army basic trainees. Each of the EPICONs has carefully validated the findings of military medical researchers of the 1950's, 1960's, and 1970's, that resumption of the oral adenovirus vaccine is the only efficacious method to control adenovirus outbreaks. This current EPICON will also make a secondary recommendation to improve the coordination between post, medical, and line officers to optimize the ventilation and sanitation systems of the 'starship' barracks buildings.

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1. REFERENCES: Appendix A contains references used in this report.
2. HISTORICAL PERSPECTIVE ON ADENOVIRUS AND ACUTE RESPIRATORY DISEASE IN THE MILITARY.

a. Acute respiratory diseases (ARD) have significantly diminished the effectiveness of the American military since its inception [2]. The modern epidemiology of ARD began in the midst of World War II (WWII), by members of the Commission on Acute Respiratory Diseases at Fort Bragg, NC [3]. Prior to WWII, however, Dunham discussed the notion that recruits experienced an unusually high incidence of ARD as compared to “seasoned” troops [4]. Factors such as the congregation of persons from disparate geographic sites and socio-economic backgrounds, overcrowding, poor ventilation, physical and mental stress, and lack of pre-existing immunity were found to predispose service members, especially recruits, to epidemics of ARD [3].

b. A suspected viral cause of ARD was first recovered from surgically removed human adenoids by Rowe *et al* and reported in 1953 as the “adenoid degeneration (AD) agent” [5]. Shortly afterward, Hilleman and Werner independently reported the isolation of “respiratory illness agents” during an ARD outbreak among recruits at Fort Leonard Wood, MO [6]. In 1956, a committee chaired by Enders recommended the name of ‘adenoviruses’ for this collection of related viruses [7]. Since that initial isolation, over 100 serotypes of adenovirus have been recognized; at least 42 infect humans with serotypes 1 through 7 the most prevalent [8]. The virus infects epithelial cells lining respiratory and enteric organs causing respiratory tract infections, conjunctivitis, hemorrhagic cystitis, and gastroenteritis. With the advent of tissue culture and serologic testing, adenovirus illness was recognized to be the most commonly occurring cause of ARD among military recruits [3]. Interestingly, outbreaks of ARD due to adenovirus are reported rarely in civilian populations [9].

c. Adenoviruses belong to the family *Adenoviridae* and are spread exclusively by human-to-human transmission via aerosolization, direct contact or the fecal-oral route; there are no known animal reservoirs [8]. Adenoviruses commonly infect children and less commonly adults. Serotypes 4 and 7 most commonly infect military recruits causing respiratory disease since the prevalence of antibody to these two serotypes is low in young adults [8]. Common respiratory symptoms are fever, rhinitis, pharyngitis, cough, and conjunctivitis. There is no specific treatment for adenovirus-associated disease.

d. Due to their significant impact on readiness, the control and prevention of ARD have held a high priority within the Army Medical Department. One of the most successful interventions was the development of adenovirus vaccines by both the National Institutes of Health (NIH) and military scientists [10-14]. These live, enteric-coated vaccines produced an asymptomatic infection with immunity to adenovirus types 4 and 7 [11,12]. Prior to the use of the vaccine in 1971, adenoviral infections caused the hospitalization of 10% of military recruits, 90% of their hospitalizations for pneumonia, and more than two-thirds of all respiratory disease in basic training [15-18]. Universal immunization with adenovirus vaccine reduced basic training hospital admissions by 95% and ARD rates by more than 50%; outbreaks in basic training due to adenovirus ceased to be a concern [11-12,14].

e. In the mid-1990's, availability of adenovirus vaccine became sporadic. At that time, military medical officers with a historical appreciation of adenoviral infections warned of the ARD outbreaks to come [18-21]. The first well-documented outbreak of adenovirus type 4 disease associated with a lack of vaccine availability occurred at Fort Jackson, SC, in the spring of 1995 [22]. One year later, the sole manufacturer of adenovirus vaccine (Wyeth-Ayerst Laboratories, Inc., Philadelphia, PA) ceased production [19]. The U.S. Army then began to ration the remaining supplies of vaccine, immunizing recruits only during the high-risk ARD season (October - March). ARD rates then rose at basic training sites across the U.S. Army in 1996-97, with large outbreaks averted by this selective immunization [18,22,23]. Nevertheless, ARD surveillance data from Fort Jackson, SC, Fort Gordon, GA, and the U.S. Naval Training Center at Great Lakes, IL, documented ARD rates as high as 10% per week in affected units [24].

f. The last U.S. Army stocks of adenovirus vaccine were used in April of 1998 [22]. Due to rising ARD rates and adenovirus outbreaks, greater emphasis was placed on non-vaccine ARD interventions (NOVARDIs). These interventions included regulations on troop density in sleeping quarters, sleeping with bunks arranged 'head-to-toe,' and enforcement of personal hygiene measures such as handwashing. Strict adherence to industry standards for heating, air-conditioning, and ventilation systems in the basic trainee barracks was also recommended. Although these industry standards are not based on health-related outcomes, poor indoor air quality in the modern, energy-efficient ("starship") barracks has long been associated with increased ARD rates [25].

3. INTRODUCTION TO THE OUTBREAK.

a. Fort Benning, GA, is the home of the U.S. Army Infantry; its primary mission is the initial and advanced training of infantry soldiers. At any given time, 6,000 to 8,000 recruits may be engaged in Infantry basic combat training (BCT) at the Sand Hill training area. The training schedule lasts 13 weeks, whereupon successful completion, the soldiers are assigned to advanced Infantry training. Additionally, Fort Benning is the home of the U.S. Army Airborne and Ranger schools.

b. The Sand Hill training area is composed of eight different battalions, each containing a total of 400 to 1000 individuals. The battalions are further divided into companies, generally five (A, B, C, D, and E) per battalion. Prior to being assigned to a

company within a battalion, all new Infantry recruits are temporarily stationed at the 30th Adjutant General (AG) where they remain for 1 to 6 weeks (average: 3 weeks). Vaccinations, an antibiotic injection, and blood typing and screening for acquired human immunodeficiency virus are some of the procedures performed upon entry to the 30th AG. When one company successfully completes the 13-week training schedule and graduates, thus vacating the battalion, a new group of recruits is subsequently moved from the 30th AG and assigned to that company.

c. On 25 April 2000, CPT Bryan J. Alsip, Chief, Preventive Medicine Services, Martin Army Community Hospital (MACH) at Fort Benning, received a call from the executive officer (XO) of the 2nd Battalion, 47th Infantry Regiment (2/47). The XO was concerned that seven trainees from a single company (A) of 2/47 had been admitted to MACH for flu-like symptoms. CPT Alsip immediately began an investigation, which included dispatching Mr. Richard Townsend, an industrial hygienist, to evaluate the barracks. Due to a concomitant investigative study with the Naval Health Research Center (NHRC) evaluating rapid nasal swab diagnostic tests for influenza A and B (FLU OIA[®], BioStar Inc., Boulder, CO and QuickVue Influenza Test[®], Quidel Corp., San Diego, CA), CPT Alsip was able to perform rapid tests on five of the admitted trainees. Four of the five tests were reported as positive for influenza A/B (influenza immunization status of the five recruits is unknown). On the morning of 27 April 2000, the technician performing the rapid tests, Ms. Sandra Williams, called to report more than 20 recruits were being evaluated at Troop Medical Clinic (TMC) #7 for respiratory symptoms and fevers greater than 100.4°F (38°C). CPT Alsip directed that they also be tested with the influenza rapid diagnostic test; 19 of 20 were reported as positive. Eighteen recruits within this population of 20 had been immunized against influenza for the 1999-2000 season; vaccination status for the remaining 2 recruits is unknown.

d. On the evening of 27 April 2000, the MACH Emergency Department was overwhelmed with approximately 70 recruits, primarily from the 2nd Battalion, 58th Infantry Regiment (2/58), complaining of respiratory symptoms and fever. As it is customary to place trainees with febrile respiratory illness at observed bed rest ('on quarters'), the number of patients requiring observation exceeded MACH's capacity. Two, 60-man sleeping bays within the 2/58 'starship' barracks (the most heavily affected unit) were converted into sick bays to house the overflow. These particular sick bays were continuously staffed with enlisted nursing personnel from MACH. Physicians from the MACH family practice service evaluated patients each morning. COL James L. Beson, Commander, MACH, directed a complete industrial hygiene inspection of all barracks in the Sand Hill training area. CPT Alsip, under the direction of COL Beson, requested formal consultation by the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) Epidemiologic Consultation (EPICON) Service on 28 April 2000 to help with the investigation and containment of the outbreak.

4. COMPOSITION AND DEPLOYMENT OF THE EPICON TEAM.

a. USACHPPM Personnel.

- (1) LTC Brian Feighner, MD, MPH, physician epidemiologist (team leader)

(2) Dr. Tracy DuVernoy, DVM, MPH, veterinarian epidemiologist

(3) Ms. Nikki Jordan, MPH, epidemiologist

b. Walter Reed Army Institute of Research (WRAIR) Personnel.

(1) MAJ Rodney Coldren, MD, MPH, Resident, Preventive Medicine Program

(2) Dr. Leonard Binn, PhD, laboratory scientist

c. MACH Personnel.

(1) CPT Bryan J. Alsip, MD, MPH, Chief, Preventive Medicine Service (PMS)

(2) CPT Rodney Gonzalez, MD, Resident, Family Practice Program

(3) Mr. Richard Townsend, MPH, Chief, Industrial Hygiene Section, PMS

(4) Mrs. Sandra Williams, LPN, laboratory technician and research assistant

d. The USACHPPM and WRAIR personnel (less Dr. Binn) joined the MACH EPICON team members on 30 April 2000.

5. OBJECTIVES OF THE EPICON TEAM.

The EPICON team's primary objective was to determine the cause(s) of the acute respiratory disease outbreak in order to control its impact on the Fort Benning community and decrease the likelihood of a recurrence. A secondary objective, should the outbreak prove to be due to influenza as initially suspected, was to determine the implications of the outbreak to the military and the nation.

6. MATERIALS AND METHODS.

Upon arrival at Fort Benning, the team met with CPT Alsip and proceeded to building 3425, the 2/58 starship barracks. The physicians interviewed and examined some of the ARD patients in the converted sick bays. A formal EPICON logbook documented the following steps in the investigation:

a. Study case definition: For purposes of our investigation, a case was defined as any trainee in the Sand Hill training area who was admitted either to MACH or the starship barracks, or who visited an outpatient clinic, with a documented oral temperature greater than or equal to 100.4°F (38°C) and at least one respiratory symptom (rhinitis, sinus pain, chest pain, cough, dyspnea, tinnitus, hoarseness, sore throat, wheezing, aural pain/ache, or ocular discharge) between 23 April and 6 May 2000.

b. Administrative data collection: Population rosters of the entire Infantry Training Brigade (ITB) were obtained to determine denominator data. Alphabetic rosters of all individuals within the two companies (B and D) of the most affected battalion (2/58) were copied and reviewed to assist with the enrollment of individuals within the case-control study. Names and telephone numbers of key battalion staff were obtained in addition to the weekly troop strength of the entire Sand Hill training area. Maps of the city, post, and training areas were also procured. The training schedules of the affected battalions were obtained and reviewed with battalion staff. The in-processing of new arrivals to BCT at Fort Benning was discussed with 30th AG staff. Particular scrutiny was given to the medical inprocessing, specifically the influenza immunization records of recruits.

c. ARD surveillance data collection: The MACH Preventive Medicine Service, in conjunction with the USACHPPM Directorate of Epidemiology and Disease Surveillance (DEDS) and the NHRC, has been recording weekly ARD rates at the Sand Hill training area for several years. An ARD case for this surveillance system is any trainee admitted to MACH for an ARD; the presence of fever is a prominent factor in the decision to admit. Additionally, a small sample of ARD patients had been routinely cultured for viral respiratory pathogens for the past 2 years as part of a Febrile Respiratory Illness (FRI) surveillance program with NHRC; the data of the culture results were collected.

d. Clinical data collection: Using unit records, medical records, and MACH administrative records, a roster of all trainees admitted to MACH or the converted sick bays in building 3425 between 23 April and 6 May 2000 was constructed. Care was taken to ensure that ill recruits were counted only once regardless of whether they were re-admitted to MACH or admitted to MACH with subsequent recovery in the sick bays. MACH medical personnel drew complete blood counts (CBC) and collected bacterial throat cultures, rapid influenza tests, viral nasopharyngeal and throat cultures, and sera on a subset of those admitted. Additional laboratory tests and procedures, such as chest radiographs, were performed if clinically indicated. EPICON team members collected viral throat cultures on those hospitalized patients who had not been previously sampled. Pertinent medical data from the inpatient records of all those admitted were abstracted. Convalescent sera were drawn during the week 21 May 2000 on a sample of those patients with acute serum samples.

e. Environmental data collection: Data from the industrial hygiene surveys conducted between 28-30 April 2000 were abstracted. These data, obtained from several companies, included information on the ventilation systems, air registers, air filters, and sleeping density (number of trainees per sleeping bay). Environmental data to measure indoor air quality were taken during the early morning hours in occupied sleeping bays and conducted within two separate companies and the 30th AG. Measurements of temperature (in degrees Fahrenheit), the percentage of relative humidity and indoor carbon dioxide levels in parts per million (CO₂ ppm), were measured using a calibrated Metrosonics® Indoor Air Quality Meter (Metrosonics® Inc., Rochester, NY).

f. Case-Control study data collection: To elucidate the etiology and exacerbating factors in the outbreak, a case-control study was performed. Members of the most affected company (D Company, 2/58) and a 50% random sampling (using the terminal digit of the

social security number) of a less-affected company (B Company) in the same battalion were enrolled. The second company was included to prevent over-matching on certain exposure variables. In addition to the data described above, a questionnaire was administered to all enrolled subjects to obtain demographics, training history, pertinent medical history, environmental factors (such as presence of soap in the latrines), and smoking history (Appendix B). Additionally, outpatient records of all enrolled soldiers in the battalion were reviewed and abstracted of information such as date of first outpatient ARD visit, symptoms, immunization history, and the maximum recorded temperature. To maintain consistency throughout the investigation, a case was defined as an Infantry basic trainee with a respiratory symptom and a documented oral temperature greater than or equal to 100.4°F (38°C) between 23 April and 6 May 2000. All other enrolled soldiers were used as controls.

g. Laboratory methods: Serologic testing for influenza A and B and adenovirus was performed in a blinded fashion by the Centers for Disease Control and Prevention (CDC) and WRAIR collaborators. Additionally, the CDC performed further testing to detect parainfluenza 1, 2, and 3, and respiratory syncytial virus (RSV) on a subset of samples. NHRC personnel performed all viral culturing and serotyping for both adenovirus and influenza viruses.

(1) Influenza rapid diagnostic tests:

(a) FLU OIA® (BioStar, Inc): “this ‘Optical ImmunoAssay’ can detect influenza A or B nucleoprotein in nasopharyngeal swabs, throat swabs, sputum and nasal aspirates. It requires eight steps and takes 15 to 20 minutes, which includes some waiting time. A blue circle due to changes in the optical properties of a silicon wafer that binds antigen-antibody complexes indicates a positive result. Using viral culture, direct immunofluorescence assay (DFA) and polymerase chain reaction (PCR) as standards, the sensitivity of the FLU OIA was 77% and the specificity was 93%.” [26]

(b) QuickVue Influenza Test® (Quidel Corp.): “an immunoassay that uses monoclonal antibodies to detect viral nucleoprotein, the QuickVue test requires mixing a nasal swab or aspirate into a solution that disrupts viral particles. A test strip containing the detection reagent is then added to the solution for 10 minutes; a pink-to-red line appears if the sample contains influenza A or B antigens. Using viral culture as the standard, QuickVue, according to the manufacturer, showed 73% to 81% sensitivity and 95% to 99% specificity.” [26]

(2) Adenovirus and influenza cultures: Sterile Dacron-tipped swabs were used to obtain nasopharyngeal viral cultures from ill recruits complaining of respiratory symptoms with a duration of 72 hours or less. If ARD symptoms were present greater than 72 hours, throat cultures for virus isolation were obtained. Cultures were placed in refrigerated viral transport media and vortexed according to published guidelines [27]. Following inoculation into Rhesus monkey kidney and A549 cells, the viral samples were incubated and observed for cytopathic effects and hemadsorption between the 5th and 7th day. If either change was observed, immunofluorescence was performed with a respiratory panel consisting of monoclonal antibodies specific to influenza A, influenza

B, parainfluenza 1, 2, and 3, respiratory syncytial virus, and adenovirus. Presence of immunofluorescence was indicative of the particular virus.

When adenovirus was identified, serotyping was performed using type-specific rabbit sera to prototype adenoviruses 1-5, 7, and 21.

(3) Influenza serology: All acute and convalescent blood samples were centrifuged after collection, and sera were aliquoted and immediately frozen at -70°C at MACH laboratory facilities. Hemagglutination inhibition measures the ability of strain-specific antibodies to prevent the agglutination of RBCs by influenza viruses [28]. The vaccine antigens used in this test were the 1999-2000 vaccine antigens: A/Sydney/5/97 (H3N2), A/Beijing/262/95 (H1N1), and B/Yamanashi/166/98. Only those specimens that demonstrated a four-fold or higher increase between acute and convalescent hemagglutination inhibition titers were considered influenza antibody positive.

(4) Adenovirus antibody detection assays: A tube dilution neutralization test in A549 cells was used to detect adenovirus-specific antibodies [27]. In this test, two-fold dilutions of heat-inactivated test serum from 1:4 and greater were tested in duplicate for neutralization of 25 to 100 CCID₅₀ (cell culture infectious dose, 50%) of virus. (Virus-serum reaction is allowed to incubate for one hour at 37°C before inoculation of cell cultures.) The endpoint titer is defined as the highest dilution of serum affording $>95\%$ protection against cytopathic effect in both tubes, and is read after 7 days. Only those paired specimens with an immunoglobulin G (IgG) antibody titer increase of 4-fold or greater were considered infected with type 4 adenovirus.

(5) Routine hospital tests and procedures: All other tests such as CBCs and bacterial throat cultures (using sterile rayon swabs), were performed in accordance with applicable standards and are not described further.

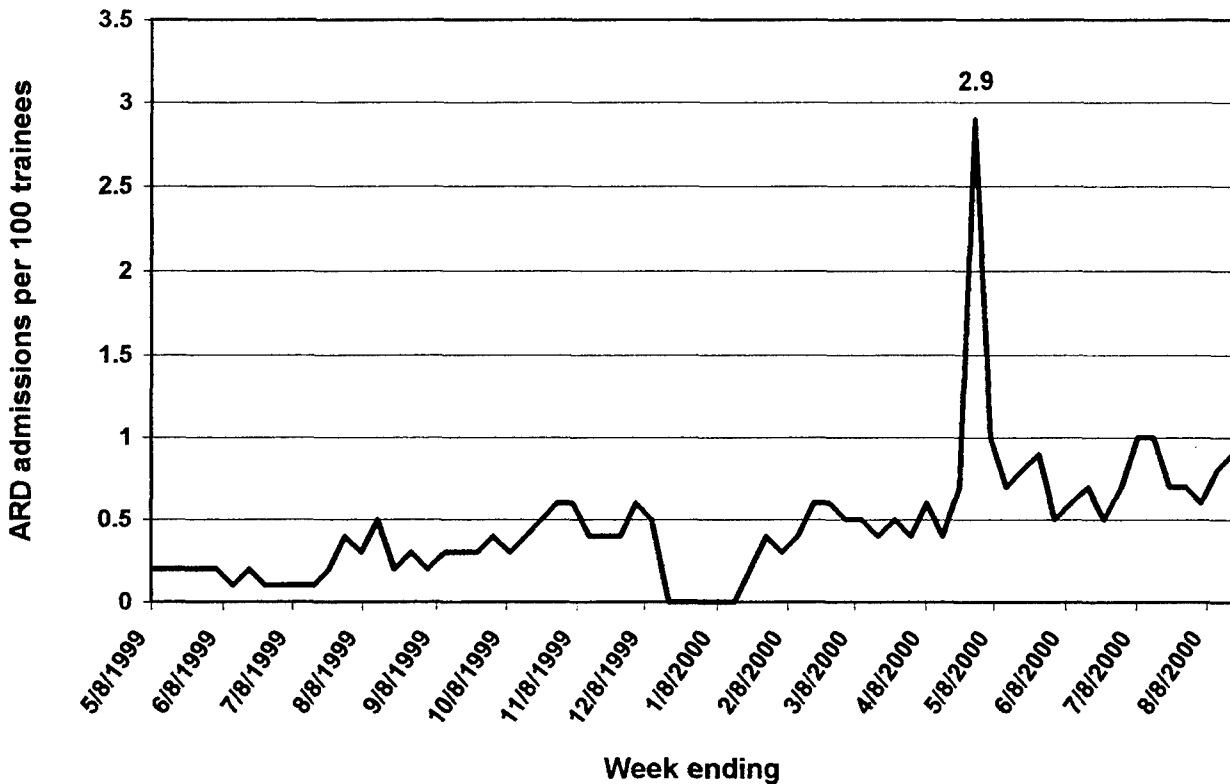
h. Data analysis: Data were coded in a computer database utilizing existing software (SPSS version 10.0, SPSS Inc., Chicago, IL). Statistical analysis of the data was performed with both SPSS and Stata (Stata 6.0, Stata Corp., College Station, TX). Binary logistic regression was performed; odds ratios (OR) as a measure of relative risk and associated 95% confidence intervals (95% CI) were estimated. Referent groups consisted of all remaining individuals without the trait of interest. Means were compared using an independent T test. Variables initially found to be statistically significant ($p < 0.05$) on univariate analysis were subsequently assessed using multivariate logistic regression. All significance testing (p values) was performed in a two-sided fashion.

7. RESULTS.

a. A total of 194 basic trainees were placed 'on quarters' to MACH or the starship sick bays with ARD symptoms between 23 April and 6 May 2000; the average length of stay was 2.1 days. This yielded an admission rate of 2.9% for the week ending 29 April 2000, a six-fold increase over baseline (Figure 1). Of the 194 admissions, 127 occurred between 27-28 April 2000 (Figure 2). ARD rates differed dramatically by unit (Table 1). Due to the concentration

of disease in one unit (2/58), it was chosen for a more detailed investigation (the case-control study). Consultation with post, county, city, state, and the CDC indicated the outbreak was localized to the Sand Hill training area of Fort Benning.

Figure 1. ARD Hospitalization Rates at Fort Benning 1999-2000.



b. Among the hospitalized recruits, 107 individuals (55.2%) had a documented oral temperature of 100.4°F (38°C) or greater, therefore satisfying our case definition. Frequency distribution of symptoms of the 107 case-patients was typical of adenoviral infections (Table 2). Fever, coughing and sore throat were the most frequently reported symptoms. A positive bacterial throat culture (presence of Group A beta-hemolytic streptococci) was present in 7 of 86 obtained, and no trend toward leukocytosis or leukopenia was noted. The average length of stay 'on quarters' for the 107 case-patients was 2.63 days, yielding 281 person-days lost. All recruits recovered without apparent sequelae. Despite the substantial number of person-days lost, all recruits completed their Infantry training and graduated on time.

Figure 2. Epidemic Curve.

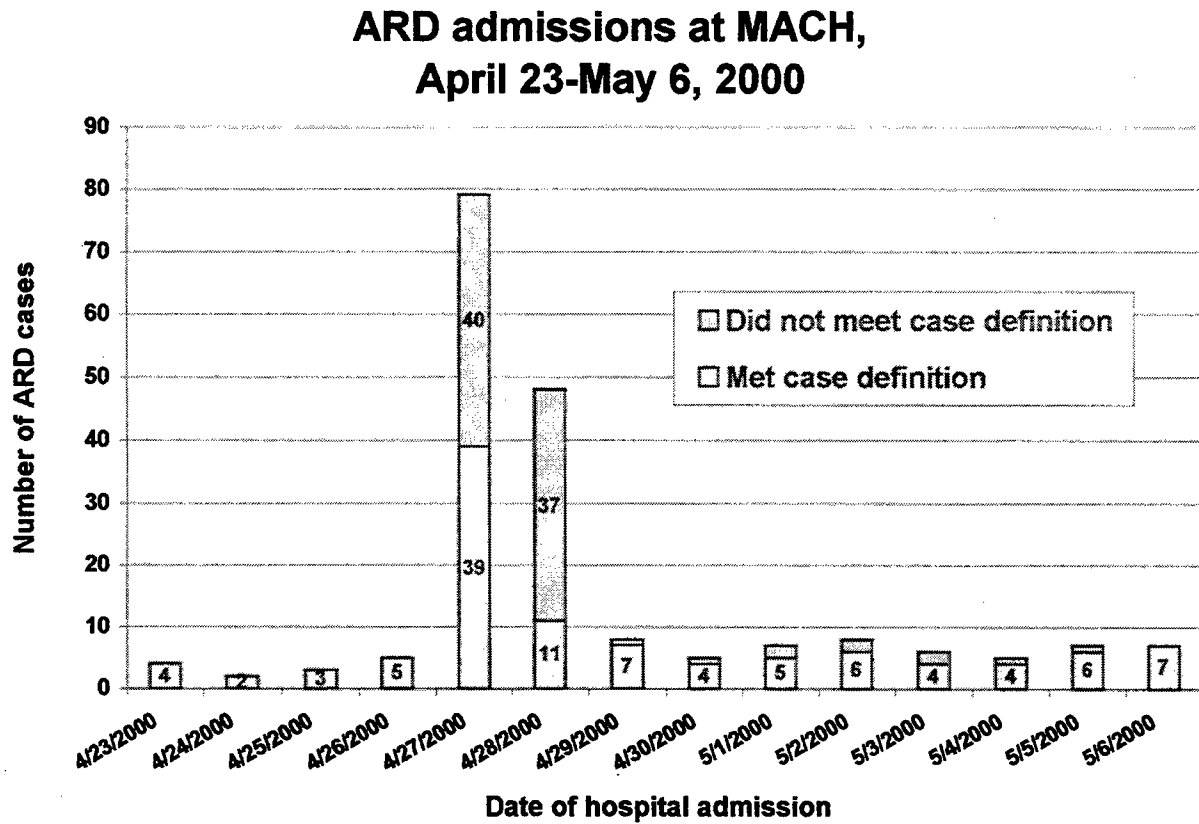


Table 1. ARD rates by unit, Fort Benning, GA, April-May 2000.

Battalion	Number of Infantry trainees hospitalized	Total trainee population	Attack rate (%)
2/58	128	999	12.8
2/19	23	812	2.8
1/19	10	396	2.5
2/47	20	877	2.3
1/38	7	806	0.9
1/50	0	816	0
2/54	0	489	0
3/47	0	473	0
Other	3	-	-
Unknown	3	-	-
Total	194	5668	3.4

c. The environmental inspection of the barracks on Sand Hill documented and photographed problems with ventilation systems (air handlers) not turned on, and dirty or missing air filters. CO₂ measurements in uncrowded sleeping bays varied from 731 ppm in sleeping bays with clean filters and running ventilation systems, to 1534 ppm in crowded sleeping bays with dirty filters. Levels of CO₂ greater than 1000 ppm are associated with inadequate ventilation and can be associated with symptoms such as headache, fatigue and upper respiratory infections [29].

Table 2. Frequency of Symptoms among Hospitalized Recruits.

Distribution of ARD symptoms among hospitalized Infantry trainees, MACH, Fort Benning, GA, April 23-May 6, 2000		
Symptom	Frequency (%) among all Infantry trainee admissions (n=190)*	Frequency (%) among admitted Infantry trainees who met case definition (n=107)
Fever	147 (77.4)	104 (97.2)
Cough	165 (86.8)	90 (84.1)
Sore throat	166 (87.4)	87 (81.3)
Headache	116 (61.1)	72 (67.3)
Rhinitis	143 (75.3)	69 (64.5)
Myalgia	113 (59.5)	69 (64.5)
Dizziness	76 (40.0)	45 (42.1)
Sinus pain	75 (39.5)	38 (35.5)
Stiff neck	56 (29.5)	26 (24.3)
Hoarseness	63 (33.2)	24 (22.4)
Dyspnea	56 (29.5)	22 (20.6)
Runny eyes/Coryza	35 (18.4)	17 (15.9)
Aural pain/ache	33 (17.4)	17 (15.9)
Chest pain	37 (19.5)	15 (14.0)
Tinnitus	28 (14.7)	13 (12.1)
Wheezing	29 (15.3)	12 (11.2)

* hospital records missing on 4 recruits

d. The review of medical inprocessing at Fort Benning demonstrated excellent procedures and solid documentation of immunizations.

e. The case-control study group included 288 basic trainees; all were male with an overall mean age of 20.7 years. Fifty-four individuals met our case definition and 234 recruits were considered non-cases or controls (Table 3). The cases were significantly younger with a mean age of 19.8 years compared to the controls, 20.9 years ($p < 0.001$). Tables 3 and 4 list the results of univariate analysis indicating several variables associated with being an acute respiratory disease case such as assignment to Company D, young age (≤ 20 years), white race, a history of smoking 6 months prior to training, 5th week of training, recruit crowding in the barracks (≥ 50 recruits per bay), higher environmental temperature ($> 72^\circ\text{F}$), lack of soap in the barracks, date of influenza immunization, and date of arrival at Fort Benning. The risk of developing ARD in Company D was almost 5 times greater than in Company B. Individuals with a history of smoking during the previous 6 months of the outbreak had twice the risk of non-smokers of developing ARD. Additionally, individuals assigned to the crowded and warmer barracks had 5 to 9 times the risk, respectively, of developing ARD compared to those assigned to cooler, less crowded barracks. Rank, availability of hot water in the barracks latrine, history of asthma, and CO_2 levels were not found to be significant (some data not shown).

f. Multivariate analysis using a forward stepwise approach of the variables from binary logistic regression with a $p < 0.05$, revealed only sleeping density greater than or equal to 50 trainees per bay ($\text{OR} = 4.1$, 95% $\text{CI} = 1.4\text{--}12.1$), and white race ($\text{OR} = 4.1$, 95% $\text{CI} = 1.2\text{--}14.2$) to be statistically significant with becoming an ARD case. Because ventilation predicted case status perfectly (no cases came from bays with operating air handlers), it could not be included in the model and no odds ratio could be calculated. Three additional variables were removed due to collinearity: week of training, low humidity level, and date of influenza immunization. The remaining variables were not significantly associated with case status in the multivariate model.

g. During the outbreak, nasal rapid tests for influenza A/B were positive in 31 of 46 (67.4%) ARD patients tested. Additionally, 46 viral cultures were obtained from 45 ill recruits during this same time period; 26 were nasopharyngeal swabs and 20 cultures were obtained from the throat. Most cultures (78.3%) were positive for adenovirus; the only subtype identified was type 4 (Adv 4). An enterovirus was cultured from eight of the remaining samples and two were negative for any viral growth. One individual had a positive adenovirus culture on both nasal and throat swabs. No influenza virus was identified in any of the cultures that were collected during the outbreak and submitted to NHRC.

h. The incongruous results between the nasal quick tests and the cultures from NHRC prompted the CDC to request paired sera (acute and convalescent) from those ill during the outbreak to detect antibody to influenza virus. Convalescent sera were obtained during 22-23 May 2000, approximately 3 weeks following the collection of acute sera. Fifty-eight acute (S1) and 40 convalescent (S2) serum samples were obtained from recruits involved in the outbreak, yielding 40 paired sera for hemagglutination inhibition (HI) testing. The missing convalescent samples were due to graduation from BCT (12), leaving the Army (4), absent without leave (1), or non-cooperation (1). Of the paired sera tested by the CDC, only one pair demonstrated an increase in antibody titers to B/Yamanashi/166/98 virus between acute and convalescent sera (HI titers: S1=1:20 and S2=1:160). None of the other 39 pairs demonstrated

a four-fold or higher increase between S1 and S2 in HI titers to any of the tested influenza antigens.

Table 3. Selected variables of Case-Control study (statistically significant unadjusted odds ratios are in bold).

Variable		Cases (n=54) No. (%)	Controls (n=234) No. (%)	Unadjusted Odds Ratio (95% CI) Cases X Controls
Age, in years	Mean	19.8	20.9	NA
	Median	19.0	20.0	NA
	Range	17-25	17-30	NA
Gender	Male	54 (100)	234 (100)	**
Race	White	48 (88.9)	167 (71.7)	3.2 (1.3-7.7)
	Black	2 (3.7)	17 (7.3)	0.3 (0.1-0.8)
	Hispanic	2 (3.7)	27 (11.6)	0.3 (0.1-0.8)
	Other	2 (3.7)	22 (9.4)	0.3 (0.1-0.8)
Residence prior to BCT	US	53 (100)	220 (96.9)	**
	Guam	0 (0)	3 (1.3)	**
	Puerto Rico	0 (0)	3 (1.3)	**
	Other	0 (0)	1 (0.4)	**
Smoker	Never	17 (31.5)	116 (50)	0.5 (0.2-0.9)
	Recent history:	-	-	2.2 (1.2-4.1)
	<= 1 pack/day*	31 (57.4)	85 (36.6)	2.5 (1.2-5.1)
	> 1 pack/day*	6 (11.1)	31 (13.4)	1.3 (0.4-4.0)
Date of flu vaccination	Jan. 2000	1 (1.8)	0 (0)	**
	Feb. 2000	1 (1.8)	3 (1.4)	1.3 (95% inaccurate)
	March 2000	52 (96.3)	212 (97.7)	0.6 (0.1-4.7)
	Other	0 (0)	2 (0.9)	**
Training unit (Company)	B	5 (9.3)	76 (32.5)	0.2 (0.1-0.6)
	D	49 (90.7)	158 (67.5)	4.7 (1.8-12.3)
Week of training	4	1 (1.9)	7 (3)	0.6 (0.03-5.1)
	5	48 (88.9)	150 (64.7)	4.4 (1.8-10.6)
	6	5 (9.3)	75 (32.3)	0.2 (0.07-0.6)
Ventilation System	On	0 (0)	19 (8.1)	**
	Off	48 (88.9)	212 (90.6)	**
	Unknown	6 (11.1)	3 (1.3)	**

* within the past 6 months, compared to those who had never smoked.

** odds ratio cannot be calculated because zero number of cases or controls were associated with this variable.

i. Many individuals in the group demonstrated a high level of antibodies against all three 1999/2000 influenza vaccine components: 87.5% had titers greater than or equal to 1:40 against A/Sydney/5/97 (H3N2), 95% had titers greater than or equal to 1:40 against A/Beijing/262/95 (H1N1) and 97.5% had titers greater than or equal to 1:40 against

B/Yamanashi/166/98. Geometric mean titers (GMT) were: 146 against H3N2, 144 against H1N1, and 238 against B vaccine components. The GMT against B/Beijing/243/97, which is not a current vaccine component, was only 21. These data demonstrate that the recruits responded well to the 1999/2000 influenza vaccine.

Table 4. Univariate results to determine which variables of case-control study were associated with case status.

Variable	Odds Ratio	95% Confidence Interval	P value
Temperature in bay >72°F	9.0	1.2-67.0	0.009
>= 50 trainees per bay	5.3	2.0-14.1	<0.001
History of asthma	2.3	0.9-5.9	0.088
Arrived at Ft. Benning after March 19, 2000	2.8	1.4-5.7	0.004
Age: ≤ 20 years	2.0	1.1-3.9	0.03
Lack of soap in barracks	2.0	1.0-4.0	.05

j. Laboratory results, including viral culture results, among the 40 individuals who provided the paired sera are presented in Table 5. Thirty-seven of 40 (92.5%) paired serum samples submitted to WRAIR for adenovirus type 4 serum neutralization testing demonstrated a 4-fold or greater increase between the acute and convalescent titers. The three remaining paired samples had an acute titer of either 1:32 (1) or greater (2) with a convalescent titer of 1:32 (2) or 1:64 (1). This lack of conversion may indicate that the three individuals had their S1 blood drawn during their initial rise in titer or they were infected with a serotype of adenovirus other than type 4. Upon submission of these three acute serum samples to NHRC for adenovirus serotyping, two of the individuals were culture-positive for adenovirus type 4 and one was culture-positive for adenovirus type 2. Among this group of individuals, 16 nasopharyngeal and 25 throat cultures were submitted to NHRC; 11 individuals had both cultures performed. Fifteen nasopharyngeal (93.8%) and all of the throat cultures (100%) were positive for adenovirus. Only one individual had a nasopharyngeal culture that was negative for adenovirus but had a positive throat culture; the remaining duplicate culture results concurred. None of the cultures were positive for influenza A or B.

k. These data strongly support the conclusion that adenovirus type 4 was the etiologic agent of this acute respiratory disease outbreak at Fort Benning, GA.

Table 5. Laboratory results among individuals who provided paired sera.

	Number of individuals tested	Number Positive (%)
Antibody status, 4-fold or greater seroconversion to:		
Adenovirus type 4	40	37 (92.5)
Influenza type A	40	0 (0)
Influenza type B	40	1 (2.5)
Adenovirus culture:	30	
Nasopharyngeal	16#	15 (93.8)
Throat	25#	25 (100)
Influenza A/B culture:	30	0 (0)
Rapid Influenza Test*:	25	25 (100)

some individuals had both nasopharyngeal and throat cultures performed.

* either FLU OIA®, BioStar, Boulder, CO or QuickVue Influenza Test®, Quidel Corp., San Diego, CA.

8. DISCUSSION.

a. This EPICON involved an ARD outbreak in a military recruit population. The epidemic curve (Figure 2) is representative of a point-source outbreak; ARD cases appear quickly with a subsequent rapid decrease in the number of cases. This phenomenon, which is somewhat uncharacteristic of contagious respiratory illnesses, may have been due to a 'cohorting' effect involving D company. Most Infantry training companies rarely interact with other companies in the same battalion; thus, they exist as small, isolated cohorts. The companies train together, eat together, and attend class together with minimal interaction among the other training companies. This 'cohorting' effect could be advantageous in certain disease situations to minimize the impact of disease upon others.

b. Of high initial interest was the specter of an influenza outbreak in appropriately immunized trainees. In the end, however, this EPICON report is simply another in a long line of reports concerning the most common cause of ARD morbidity in military recruits - adenoviruses.

c. In the preceding year (12 April 1999 to 19 April 2000), of the 482 throat and nasopharyngeal cultures sent to the Emerging Illness Division of NHRC, as part of their surveillance of FRI in the military, one-half of the ARD cases at Fort Benning were due to adenovirus. The only subtype identified was adenovirus type 4 (10 of 10). During the same time period only four submissions from Fort Benning were culture positive for influenza A, the only subtype isolated was H3N2. Interestingly, 47 of 62 (75.8%) of the ARD samples cultured

within the month prior to the outbreak (22 March to 19 April 2000) were also positive for adenovirus.

d. One reason for the significant number of false positive results in association with the rapid influenza tests may have been due to cross reactivity of adenovirus type 4 to influenza A/B. The package insert of each brand of influenza quick test stated that cross reactivity did *not occur* with adenovirus type 5 or 7a; there was no discussion of cross reactivity involving Adv type 4, the etiologic agent associated with this outbreak. However there is no known antigenic relation between adenovirus type 4 and influenza and probably indicates a false test result for unknown reasons. According to representatives from both manufacturers, influenza vaccine-induced antibody will not cause false-positive results since both quick tests detect antigen. Inconsistencies between laboratory technicians performing the rapid influenza test are probably not a factor for the spurious results since only one technician (SW) was responsible for obtaining, performing, and interpreting all of the rapid tests.

e. At the outbreak to Fort Benning officials, the epidemiologic triad of agent-host-environment was used to discuss how ARDs affect populations. Each of the parts of the triad affect the severity of outbreaks and each may be modified to reduce disease. The agent, adenovirus type 4, has been known as a cause of acute respiratory disease within military populations for decades. There is no reason to expect adenovirus to disappear from military recruit populations. The host, in the past, was modified by adenovirus vaccine. The vaccine eliminated ARD outbreaks due to adenovirus. Adenovirus vaccine is presently unavailable and that status will not change for several years. Until adenovirus vaccine is once again available, outbreaks due to adenovirus in basic training are inevitable. Other host modifications, such as tobacco cessation, are helping to decrease ARD. The environment, specifically air quality in the barracks sleeping bays, also had a part to play in this outbreak. This investigation documented breakdowns in the routine maintenance of the ventilation of the starship barracks that, as noted above, have a long history of being associated with higher ARD rates. Among the three aspects of the triad, the host, specifically re-institution of adenovirus immunization, is clearly the most important. Until that time, the ventilation systems of the starship barracks are the most correctable of the contributing factors in this outbreak.

f. One reassuring finding that came as an indirect result of the investigation to rule out influenza disease was the serologic documentation of excellent immunization coverage and vaccine response in the Fort Benning recruits to this year's influenza vaccine.

9. RECOMMENDATIONS.

a. The optimal measure for preventing outbreaks due to adenovirus is immunization, as demonstrated by the successful control attained after initiation of a universal adenovirus immunization program in the early 1970's. In the absence of vaccine, military recruits are vulnerable to these infections, just as they were during earlier decades (1940's-1960's). Until vaccines are once again available, develop other approaches to inhibit the spread and minimize the costs of adenovirus infections among trainees.

b. Improve coordination between line units, the Department of Public Works (DPW), and MACH to ensure the correct operation of the ventilation systems and air exchanges in sleeping barracks, in accordance with ASHRAE standards [1]. Timely exchange of Heating, Ventilation, and Air-Conditioning (HVAC) filters within these systems, regular cleaning of vents and intakes, and consistent monitoring to ensure proper functioning of the system are necessary. Large-scale cleaning of the internal ventilation systems should be considered if otherwise well maintained systems cannot function to specifications.

c. Emphasize the continuation of other non-vaccine ARD interventions (NOVARDIs) such as hand-cleaning, personal hygiene, provision of adequate personal space (72 square feet / recruit as per Army Regulation, 40-5), and head-to-toe bunk orientation. In extreme ARD outbreaks, acquisition of additional barracks space, supplemental staff or delay in the entry of new, non-immune recruits may be necessary.

d. Consider weekly surveillance for ARD the most critical step in addressing the resurgence of this adenovirus challenge. Appropriate adenovirus surveillance should include tracking of general ARD, as well as sampling for specific pathogens among hospitalized ARD cases. Such a system is already in effect at Fort Benning and should be continued.

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APPENDIX A.

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APPENDIX B.

Fort Benning Respiratory Disease Questionnaire

Today's Date: _____ MAY 2000

Last Name _____ First Name _____

SSN _____ - _____ - _____ Age _____ Rank _____

Race: ☐ African-American ☐ Asian ☐ Caucasian ☐ Hispanic ☐ Native American ☐ Other

BN _____ Co _____ Platoon _____ Squad _____ Week of Training: _____

In what state did you live before you came to Ft. Benning? (If not USA, state country) _____

What day did you arrive at Ft. Benning (30th AG)? _____ / _____ / _____
DAY MONTH YEAR

Did you receive shots (immunizations) when you came to Ft. Benning? ☐ YES ☐ NO ☐ DON'T KNOW

Check any Symptoms you had **in the last 10 days** (check all that apply):

- | | | |
|-------------------------------------|--|---|
| <input type="checkbox"/> Fever | <input type="checkbox"/> Cough | <input type="checkbox"/> Runny/Stuffy Nose |
| <input type="checkbox"/> Headache | <input type="checkbox"/> Trouble breathing | <input type="checkbox"/> Sore Throat/Trouble swallowing |
| <input type="checkbox"/> Runny Eyes | <input type="checkbox"/> Muscle Aches | <input type="checkbox"/> Earache/Trouble hearing |
| <input type="checkbox"/> Sinus pain | <input type="checkbox"/> Ringing in ears | <input type="checkbox"/> Stiff neck |
| <input type="checkbox"/> Dizziness | <input type="checkbox"/> Hoarseness | <input type="checkbox"/> Wheezing |
| <input type="checkbox"/> Chest pain | <input type="checkbox"/> Other _____ | |

Did you go to the TMC or the hospital for any of the above symptoms **in the last 10 days**?

☐ YES ☐ NO ☐ DON'T KNOW

Have you ever had: ☐ Allergies/Hay fever ☐ Asthma

Were you put in the hospital or in the sick bay in your barracks anytime **in the last 10 days**?

☐ YES ☐ NO ☐ DON'T KNOW

Did you smoke tobacco **in the 6 months before** you came to Ft. Benning? ☐ YES ☐ NO

If YES, how much did you smoke? ☐ 1 pack/day or less ☐ More than 1 pack/day

Did you have hot water in your barracks every day **for the past 10 days**?

☐ YES ☐ NO ☐ DON'T KNOW

How many times a day did you wash your hands **in the last 10 days**?

☐ None ☐ 1-2 times ☐ 3 or more times

Did you have soap in the barracks every day **in the last 10 days**?

☐ YES ☐ NO ☐ DON'T KNOW

Were the bunks in your sleeping bay arranged 'head to toe'?

☐ YES ☐ NO ☐ DON'T KNOW